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09/684,883	10/06/2000	Bernard R. Brodeur	047998/0197	3090

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EXAMINER
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1645	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/684,883	Applicant(s) Brodeur
	Examiner Mark Navarro	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *91-181* is/are pending in the application.

4a) Of the above, claim(s) *91-123, 126, 131, 132, and 138-169* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *124, 127-130, 133-137, 170-174, 178, 180, and 181* is/are rejected.

7) ☒ Claim(s) *125, 175-177, and 179* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants amendment filed June 30, 2003 (Paper Number 14) has been received and entered. Claims 174-181 have been added. Consequently, claims 91-181 are pending in the instant application, of which claims 91-123, 126, 131-132, and 138-169 have been withdrawn from further consideration as being drawn to a non-elected invention in Paper Number 7, received May 10, 2002.

Claim Objections

1. The objection of claim 125 for reciting non-elected, independent and distinct proteins which have been withdrawn from consideration is withdrawn in view of Applicants amendment.

Claim Rejections - 35 USC § 112

2. The rejection of claims 127-129 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, a new matter rejection is withdrawn in view of Applicants demonstration of support.

3. The rejection of claims 124, 127-130, 133-137, and 170-173, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, a written description rejection is maintained. Additionally this rejection is applied to newly submitted claims 174, 178, and 180-181.

Applicants are asserting that claim 124 and all the other claims require that the polypeptide be "antigenic." Applicants assert that such a property is more than sufficient to define the "function" of the claimed polypeptides. Applicants further assert that since both a full sequence and an appropriate biological function are disclosed and claimed, withdrawal of the written description rejection is in order.

Applicants arguments have been fully considered but are not found to be fully persuasive.

First, Applicants have asserted that claim 124 and all the other claims require that the polypeptide be "antigenic." However, Applicants "function" is a property shared by every protein in the known universe. Every protein under the right conditions will react with antisera, accordingly, Applicants have not disclosed any particular function to identify members of the genus, since every protein will have Applicants claimed "function."

Second, Applicants further assert that since both a full sequence and an appropriate biological function are disclosed and claimed, withdrawal of the written description rejection is in

order. However, as set forth above, Applicants have not identified a "function" which would allow for determining members of the genus. The examples set forth in the written description guidelines show proteins with "functions" that readily identify certain members of a genus. (See for example, Example 13 where the protein has "tumor necrosis" activity.

Claims 124, 127-130, 133-137 and 170-173 recite an isolated polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to the complement of a DNA sequence encoding a Neisseria surface protein, wherein said Neisseria surface protein; is resistant to proteinase K and has an apparent molecular weight of 22 kDa, wherein said polypeptide is antigenic.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2 alone is insufficient to describe the genus. Thus, Applicant's have not described a function of the isolated polypeptide which would adequately describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Furthermore, the function of the specifically claimed fragments (e.g., amino acids 31-55 of SEQ ID NO: 2, etc.) is not set forth, the written description of the instant application is supportive of only an antigenic peptide consisting the fragment, since additional amino acids on the N-terminus or C-terminus will have a profound impact on the activity of the protein.

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The protein itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

For reasons of record in Paper Number 12, as well as the reasons set forth above, this rejection is maintained.

4. The rejection of claims 133-137 and 170-173 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine composition comprising the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for pharmaceutical/vaccine compositions comprising a polypeptide which hybridizes under stringent conditions to a DNA sequence encoding a Neisseria surface protein which is resistant to

proteinase K and has an apparent molecular weight of 22 kDa. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained. Additionally this rejection is applied to newly added claims 180-181.

Applicants are asserting that the specification discloses routine assays for determining whether the polypeptides of the invention are suitable for use as a vaccine, i.e., whether the protein confers protection against subsequent bacterial challenge (specification at page 17, lines 13-23 and Example 6 at page 51). Applicants assert that nothing more is needed. Applicants assert that the mere possibility that some surface proteins or epitopes of a given bacterium might not be sufficiently antigenic to provide immunity, as alleged by the examiner, is not enough to establish lack of enablement.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted,

however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

First, no working examples of any "hybridized" DNA encoding protein or epitope region are provided. Second, the prior art has already set forth that "The key problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies... and thus protect the host against attack by the pathogen. (See Plotkin of record). This clearly emphasis point 7, identification of "protective antigens" is anything but routine and predictable.

As for "epitopes" which provide protection, Fox (U.S. Patent Number 4,879,213) sets forth that "without knowing a protein's three dimensional structure there is no reliable method for determining which linear segments of the protein are accessible to the host's immune system" and that "whether the three dimensional structure is known or not, short linear polypeptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants." This again emphasis the point that identification of "epitopes" for protection is unpredictable.

The specification provides insufficient guidance of how to use the claimed polypeptides as a vaccine. It is well recognized in the art that it is unclear whether a single protein derived from a

pathogen will elicit protective immunity. Ellis, R.W. (see Chapter 29 of "VACCINES" [Plotkin, S.A *et al.*,(ed.), published by W.B. Saunders Company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies ...and thus protect the host against attack by the pathogen."

A vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

It is noted that Applicant's specification demonstrates protection in mice against Neisseria meningitidis strain 608B lethal challenge when vaccinated with the 22 kDa surface protein identified as SEQ ID NO: 2. (Page 52). However, this is the only working example. While those of skill in the art would recognize that the protein identified as SEQ ID NO: 2 is capable of conferring protection to mice, these results are not commensurate in scope with Applicant's claim language encompassing all proteins capable of hybridizing under undefined conditions to a protein of undefined function. Since the art teaches of the unpredictability of using a single antigen for vaccination it would be an undue burden and be unpredictable to use the broadly claimed product for vaccination.

For reasons of record in Paper Number 12, as well as the reasons set forth above, this rejection is maintained.

5. The rejection of claim 124 under 35 U.S.C. 112, second paragraph, as being vague and indefinite in the recitation of "stringent conditions." is maintained.

Applicants are asserting that exemplary hybridization conditions are detailed in the specification in Example 4 (page 46, lines 11-25).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Accordingly, the metes and bounds of the phrase "stringent conditions" cannot be determined. Furthermore, Applicants still have identified the physical and chemical conditions of the wash step of the "stringent" hybridization.

For reasons of record in Paper Number 12 as well as the reasons set forth above this rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 124, 133-137, 170 and 172 under 35 U.S.C. 102(a) as being anticipated by Merks *et al* is maintained. Additionally this rejection is applied to newly submitted claims 174 and 180-181.

Applicants are asserting that there is no disclosure or teaching that the 20 kD surface protein disclosed in Merks is resistant to proteinase K treatment or is related in any way to the 22 kD Neisseria polypeptide which is resistant to proteinase K treatment of the instant invention. Applicants further assert that Merks clearly provides insufficient disclosure to compel the conclusion that the 20 kD protein disclosed therein is the same antigen as the presently claimed polypeptide.

Applicants arguments have been fully considered but are not found to be fully persuasive.

Applicants arguments are not found to be persuasive in view of the disclosure of Merks et al.

Applicants are asserting that there is no disclosure or teaching that the 20 kD surface protein disclosed in Merks is resistant to proteinase K treatment or is related in any way to the 22 kD Neisseria polypeptide which is resistant to proteinase K treatment of the instant invention. While the Examiner agrees that Merks is silent to resistance or sensitivity to proteinase K

treatment, there is sufficient overlapping properties to suggest that the protein as claimed is the same as that disclosed by Merks. Both the protein as claimed and the protein disclosed by Merks share the following properties: obtained from Neisseria meningitidis, cell surface protein, molecular weight of about 20 kDa, antigenic. These properties alone provide sufficient evidence to suspect that they are the same. The Examiner is simply not capable of dropping the protein disclosed by Merks in proteinase K to observe if breakdown occurs. Since the Patent office does not have the facilities for examining and comparing applicants' product with the product of the prior art reference, the burden is on applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

The claims are directed to an isolated polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to the complement of a DNA sequence encoding a Neisseria surface protein, wherein said Neisseria surface protein is resistant to proteinase K, and has an apparent molecular weight of 22 kDa, wherein said polypeptide is antigenic.

Merks *et al* (WO 94/05703) disclose of a cell surface protein of Neisseria meningitidis with a molecular weight of about 20 kDa. Merks *et al* further disclose of the protein in combination with adjuvants and carriers as well as administration to an animal, and generating an antibody. (See abstract and pages 4-5).

In view that both the instantly filed application and the disclosure of Merks *et al* are surface proteins of Neisseria meningitidis with a molecular weight of about 20 kDa, and both are antigenic, the disclosure of Merks *et al* is deemed to anticipate the claimed invention.

It is noted that Merks *et al* do not characterize the protein as being resistant to proteinase K, however since the protein disclosed by Merks *et al* shares the same structural requirements as set forth in the claims, as well as being isolated from the same source, with the same molecular weight, and same property of antigenicity, the feature of being resistant to proteinase K is deemed to be an inherent property.

For reasons of record in Paper Number 12 as well as the reasons cited above, this rejection is maintained.

7. The rejection of claims 124, and 133-135, under 35 U.S.C. 102(b) as being anticipated by Bhattacharjee *et al* is maintained. Additionally this rejection is applied to newly submitted claims 174 and 180-181.

Applicants are asserting that Bhattacharjee discloses the purified H.8 surface antigen preparation exhibited three bands on an SDS-PAGE gel with a major band at 27 kD (page 776, second column and Figure 1). Applicants assert that by contrast the Neisseria protein of the instant invention has a molecular weight of 22 kd. Applicants further assert that as for SEQ ID NO: 2, it has a significantly different amino acid composition.

Applicants arguments have been fully considered but are not found to be persuasive.

Applicants argument are not found to be persuasive in view of the disclosure of Bhattacharjee et al.

First, Applicants assert that Bhattacharjee discloses the purified H.8 surface antigen has a molecular weight of 27 kD, and that by contrast the Neissera protein of the instant invention has a molecular weight of 22 kd. However, Applicants are directed to their own claim language which recites "about 22 kD." The term "about" allows a certain degree of latitude, sufficient latitude to allow a protein of 27 kD to be encompassed.

Second, Applicants assert that SEQ ID NO: 2 has a significantly different amino acid composition then the protein disclosed by Bhattacharjee. However, Applicants are again respectfully directed back to the claims. Not a single rejected claim recites any sequence.

The claims are directed to an isolated polypeptide encoded by a polynucleotide that hybridizes under stringent conditions to the complement of a DNA sequence encoding a Neisseria surface protein, wherein said Neisseria surface protein is resistant to proteinase K, and has an apparent molecular weight of 22 kDa, wherein said polypeptide is antigenic.

Bhattacharjee *et al* (Infection and Immunity Vol. 56, No. 4, pp 773-778, April 1988) disclose of a cell surface protein of Neisseria meningitidis with a molecular weight of about 22 kDa. (See abstract).

In view that both the instantly filed application and the disclosure of Bhattacharjee *et al* are surface proteins of Neisseria meningitidis with a molecular weight of about 22 kDa, the disclosure of Bhattacharjee *et al* is deemed to anticipate the claimed invention.

It is noted that Bhattacharjee *et al* do not characterize the protein as being resistant to proteinase K, however since the protein disclosed by Bhattacharjee *et al* shares the same structural requirements as set forth in the claims, as well as being isolated from the same source, with the same molecular weight, and same property of antigenicity, the feature of being resistant to proteinase K is deemed to be an inherent property.

Since the Patent office does not have the facilities for examining and comparing applicants' product with the product of the prior art reference, the burden is on applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

For reasons of record in Paper Number 12 as well as the reasons set forth above, this rejection is maintained.

Double Patenting

8. The rejection of claims 124-125, 127-130, 133-137, and 170-173 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of

U.S. Patent No. 6,287,574 is withdrawn in view of Applicants filing of a terminal disclaimer, which has been made of record.

Claims 125, 175-177 and 179 are objected to for depending upon a rejected base claim, however claims 125, 175-177 and 179 are free of the prior art of record.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro, whose telephone number is (703) 306-3225. The examiner can be reached on Monday - Thursday from 8:00 AM - 6:00 PM. The examiner can be reached on alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Lynette Smith can be reached at (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1645 by facsimile transmission. Papers should by faxed to Group 1645 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703) 308-4242.

Mark Navarro

Primary Examiner

September 10, 2003